dividual constitution varies so greatly that what is good for one may be bad for another.

Almost the only constant health rule that we find in the lives of octogenarians and centenarians is moderation. The flight surgeon is in a position to evaluate health measures and, eventually, to make reliable recommendations.

The outstanding need in medical aviation is international joint action in research, and evaluation of the various tests in use by the different countries. Many of our flight surgeons have regretted the difficulties attending coöperation between the flight surgeons of our Army and Navy; there should be some provision for exchange of flight surgeons so that constructive criticism would be provided.

In our section of the Joint Munitions Board, General Ireland and myself were in perfect agreement that the utmost coöperation must obtain in the medical departments of the two services.

In my opinion, the visit of the consulting flight surgeon of our bureau to the medical aviation centers of Europe has been of inestimable value to naval medical aviation. More progress could probably be made in a few months than in a few years if, instead of working alone, there should be the most intimate association between the flight surgeons of our Army, Navy, and Department of Commerce, and these with a similar activity of other countries of the world.

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THE ENLARGED SPLEEN*

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THE problem of the enlarged spleen frequently presents itself to the physician. In the majority of cases the signs and symptoms are confused and the clinical phenomena are not always closely related to the spleen. Physiologically the spleen is not important, but pathologically it is a menace to the patient, because splenic enlargement of itself increases a function which is not significant, to an overactivity which is not easily controlled through natural agencies.

The lymphoid tissues of the body, of which the spleen is a part, have been named by Aschoff and Landau the reticulo-endothelial system; they comprise a number of tissues with diverse functions not always related to each other. The cells of the sinuses of the spleen are closely related to the Kupffer cells of the capillaries and sinuses of the liver. These structures have in common the ability to develop lymphocytes, which form about 25 per cent of the total white blood cells, and, to a less and varying extent, the mononuclear leukocytes. The lymphocytes are produced in large numbers by the Malpighian tufts and it is probable that the production of lymphocytes is the chief function of these nodes. The lymphocyte, as pointed out by Carrel, has all the properties of growth and nutrition, which he demonstrated in the nurture under glass of fibroblastic tissue. The phagocytic action of the large mononuclear leukocytes is well marked, and these cells, with the aid of the reticulo-endothelial cells generally, remove from the blood stream and tissues subnormal red blood cells as well as microörganisms and foreign bodies—functions of the spleen which are maintained in the shadowy capillary area between the splenic arteries and veins.

The lymphoid tissues, again, are of interest because they become senescent to a greater or less extent. C. H. Mayo pointed out more than thirty years ago that the lymphatics, after the adolescent period, gradually become less active through the development of fibrous tissues, and that the reason cancer spreads less rapidly in the old than in the young is that the lymphatics of older persons are not sufficiently active to disseminate the disease quickly.

The appendix has a relatively large amount of lymphoid tissue, and undergoes normally the same type of senescence. The gradual disappearance of its lymphoid structure, with the accompanying contraction and obliteration of its lumen, has been wrongly named "appendicitis obliterans." Failure to relieve supposedly related symptoms by appendectomy has given rise to much argument with regard to the validity of chronic appendicitis.

It often happens that tonsils which are very large in youth, by middle age will have shrunk so as to be scarcely noticeable under the pillars of the fauces. The tonsils are lymphoid in structure, and perhaps one of their functions is to permit, early in disease, a few bacteria to enter the blood to stimulate resistance.

The spleen reaches the height of its activity in the adolescent period, and it is during this period that disease of the spleen is most frequntly manifest. By the age of forty, the functional capacity of the spleen has become greatly reduced, because of the introduction of fibrous tissue.

The pulp cells of the spleen are efficient phagocytes, and the phagocytic activity of the spleen as well as its strainer function in the removal of bacterial and protozoal and toxic material is aided greatly by the normal disappearance in the spleen of the outer and middle coats of the blood vessels, so that the blood comes in direct contact with the endothelial lining of the splenic capillaries and sinuses. In the dog, the spleen may contain about 20 per cent of the total blood volume, and in times of stress the blood may be forced into the circulation by the nonstriated muscle fibers of the spleen. Undoubtedly this is equally true of man, and perhaps accounts for the left-sided pain in the marathon runner. According to tradition, the ancient Greeks removed the spleen from their runners in preparation for the race.

The control of the action of the spleen apparently depends to a large extent on unidentified internal secretion, since the nerve supply to the capsule from the sympathetic system is scanty.

Our knowledge of the functions of the spleen has been deduced to a considerable extent from the clinical pathology. It has been shown that regardless of the nature of the enlargement of

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the spleen, the destructive effect on the blood becomes manifest in the form of chronic anemia.

The red blood cells are produced in the myeloblasts of the bone marrow. Mann and Magath have shown that destruction of the red cells, as far as the bile pigments are concerned, takes place largely in the bone marrow, and only to a small extent in the lymphoid tissues, and that the function of the liver is rather to filter out bile pigments than actively to destroy great numbers of red cells.

Ashby has shown that normal red blood cells may live seven weeks and probably longer. When the spleen is enlarged, its destructive function is enhanced, and it destroys red blood cells which, although they may not be normal, are still capable of functioning.

The red blood cells are the oxygen carriers, and contain one or more atoms of iron to each molecule of hemoglobin. When these cells are reduced, chronic anemia or suboxidation is a result. That the spleen may destroy a certain number of white blood cells as well as red blood cells is shown in the leukopenia of splenic anemia. In hemolytic icterus there is a specific destructive effect of the enlarged spleen on the red blood cells, which in this disease are abnormally fragile, and in hemorrhagic purpura there is specific destruction of the blood platelets, which have to do with the clotting of the blood.

One of the theories of the clotting of blood is that the blood contains a ferment called prothrombin, which tends to clot, and a second ferment, antithrombin, which prevents clotting. When there is injury to the tissues, the thromboplastin, formed from blood platelets, unites with the antithrombin, and permits the prothrombin with the calcium to form a clot. If thromboplastin is absent from the blood and tissues, due probably to increased resistance of platelets, hemophilia results; if the blood platelets are reduced, purpura results, and if the calcium is exhausted, as it sometimes is in long continued jaundice, the hemorrhagic conditions develop which sometimes accompany chronic jaundice.

The removal of the spleen in experimental animals and in cases frequently seen in man in which a normal spleen has sustained traumatic rupture, has shown that beyond the temporary effect of the operation the physical economy has not been impaired.

Grouping the disease conditions which have produced enlargement of the spleen makes apparent certain interesting data.

The four main dysfunctions of the enlarged spleen concern, first, the liver and bone marrow; second, the blood; third, the action of the spleen as a filter, and fourth, its relation to malignant disease of the spleen and other lymphoid tissues.

The liver bears a close relation to the spleen. The spleen has a large blood supply, but its veins join with the portal vein and supply about 20 per cent of the blood in the portal circulation. All the material, protozoa, bacteria, toxic substances, and the various elements that have been collected by the spleen in its capacity of a strainer eventually are carried to the liver.

The fact that the spleen is a strainer accounts for its enlargement in typhoid, tuberculosis, malaria and syphilis. In these diseases the spleen may become incapable of destroying material that it deletes from the blood. Therefore, when the material is sent on to the liver, it has not been efficiently prepared by the spleen. The material is toxic, and, although the liver is the great detoxicating organ of the body, sometimes, in late stages of the diseases mentioned, it is injured and the fibrosis (cirrhosis), which Banti described, is produced. The hepatic cells are all alike in function and therefore the morphology in a pathologic state is simple as compared with that of organs with several types of cells.

In neoplastic conditions the spleen may take part in the production of white cells of embryonic character, such as are seen in splenomyelogenous leukemia and in other diseases, for instance, Hodgkin's disease, according to some pathologists, and various types of lymphoma. It is of interest in this connection that these embryonic white cells that are produced so rapidly are destroyed readily by various agents, particularly x-ray and radium, to which all the lymphoid tissues have great sensitivity, although the disease may not be cured by this destruction. As Desjardins has pointed out, the sensitivity of the normal cells of a tissue to radium and x-ray is the index of the benefit that may be expected from the use of these agents in the cure or palliation of malignant disease of that tissue.

This short résumé of the clinical relationship of the enlarged spleen to general conditions enables broad evaluation of the results of splenectomy. I have classified 534 cases of splenectomy on the clinical rather than on the pathologic basis. I am indebted to my colleagues for important data. Dr. Giffin has worked out the clinical course of these cases as related to the condition of the blood and the diagnosis, with which he has dealt in various papers, and Dr. MacCarty has observed the pathologic condition of the spleens removed. An attempt has been made to correlate these data, but the pathologic condition is not always closely related to the clinical condition; this may well be expected, since the spleen is only one of a number of organs or tissues that are concerned.

DATA CONCERNING 534 CASES IN WHICH SPLENECTOMY WAS PERFORMED BETWEEN APRIL 1, 1904, AND APRIL 1, 1929 (TWENTY-FIVE YEARS)

Clinical Classifications	Cases	Hospital Mortality
Disease associated with abnormality of the red blood cells	207	11
Disease associated with abnormality of the white blood cells	55	3
Disease due to filtration of infectious and toxic agents	237	30
Splenic neoplasms	11	3
Miscellaneous	24	4
Total	534	51

Some of the patients who died following splenectomy recovered satisfactorily from the operation, but were not greatly benefited by it and remained

in the hospital until death occurred. For this reason the hospital mortality is given rather than the operative, which would be much less.

DISEASE ASSOCIATED WITH ABNORMALITY OF THE RED BLOOD CELLS

I shall take up the splenic syndromes associated with abnormality of the red blood cells in the order in which the results of splenectomy were the best. Of these, hemolytic icterus is first.

Hemolytic icterus.—This disease is characterized by enlargement of the spleen and the liver, by chronic jaundice, and by fragility of the red blood cells, which is rather in keeping with the idea that the spleen is an agent of destruction rather than the cause, as this fragility of the red blood cells continues after the spleen has been removed. In the uncomplicated case the ordinary signs of obstructive jaundice are not present; that is, the stool is of normal color, and bile is not present in the urine, but 68 per cent of these patients have gall stones, because of the enormous amount of bile pigment which has come from the destroyed red blood cells. These gall stones may result in irritations and infections and give rise to obstructive jaundice with the other symptoms of gall stones.

Hemolytic icterus exists in two forms, the first of which is the infantile or congenital type of Minkowski, which may be present from birth. Various members of the same family may be more or less affected by this dyscrasia. The second is the acquired type of Hayem and Widal, which is usually seen in the adolescent period. In this type the symptoms are more acute and lead to progressive anemia and death from intercurrent disease, usually by middle life or before.

The familial type of hemolytic icterus may vary from conditions in which the destructive effect is so marked as to necessitate early splenectomy, to those in which the symptoms are so slight that the disease may exist for years without causing serious injury.

The acquired type of hemolytic icterus is a more serious condition and usually requires splenectomy.

Hemolytic icterus is marked clinically by intermittent fever, or malaise, in which there is an increase of jaundice, and of tenderness about the spleen and the liver. Patients should not be operated on during acute manifestations, as the symptoms are due to acute toxemia which may result in death following operation. The mortality of splenectomy in the uncomplicated cases is low; in our series of 100 cases there were four deaths. Within four days after the operation the patient, perhaps for the first time in his life, is free of jaundice.

Hemorrhagic purpura.—In chronic hemorrhagic purpura also, splenectomy gives remarkable results. In this disease acute manifestations may sometimes develop, and the acute type should be carefully distinguished from the acute purpura of the late stages of aplastic anemia, leukemia, and dyscrasias of that type in which splenectomy does no good and gives a high immediate mortality.

In the typical case of hemorrhagic purpura the blood platelets, which ordinarily range from 250,000 to 400,000, are reduced to less than 100,000; at 80,000 mild purpura may appear, and at less than 30,000 purpura will be marked. When the blood platelets are reduced to 30,000 or less, as may happen in some acute types, the patients must be rehabilitated by transfusions and other measures before splenectomy is attempted.

In the chronic cases of hemorrhagic purpura, the purpura may be more or less intermittent. In the female, serious hemorrhages from the uterus at the menstrual time may be marked and prolonged. The spleen usually is readily palpable, but sometimes it is not large enough to be palpated.

Removal of the spleen in chronic hemorrhagic purpura acts like magic. The external wound which in the course of opening the abdomen may have required a large number of forceps on blood vessels, will often stop bleeding within a few minutes after the splenic pedicle has been tied. The spleen as a rule is not adherent and is readily removed. The mortality in our series of thirty-two cases was one.

Pernicious anemia.—In pernicious anemia the debilitated red blood cells, the best the patient can produce, may be removed by the lymphoid tissues, especially by the spleen. In the occasional case, splenectomy may be indicated, although feeding liver has greatly reduced the percentage of cases in which splenectomy would be advisable.

The removal of the spleen is at once followed by palliation much more marked and prolonged than that following blood transfusions, and the patients lived two and a half times as long as comparable patients in whom the spleen was not removed. A few of these patients are still alive, following splenectomy, after a number of years, but are not cured.

In sixty-two cases of splenectomy for pernicious anemia, there were four deaths.

Polycythemia vera.—I will speak of only one other condition and that is polycythemia vera. This disease has been so contradictory in the results of splenectomy as compared with its pathologic expectation, as to amount to a paradox.

In polycythemia vera the spleen is enlarged, the liver is enlarged, the hemoglobin varies from 100 per cent to 130 per cent, and the red blood cells may run as high as 10,000,000 or 12,000,000 in each cubic millimeter. The spleen was removed in three of these rare cases in the clinic, in one with remarkable improvement lasting now nearly eight years. The liver of this patient is still large and hard, the hemoglobin runs about 100 per cent, and the red blood cells about 6,000,000, but the patient is, to all intents and purposes, well. The second and third cases are too recent for evaluation.

DISEASE ASSOCIATED WITH ABNORMALITY OF THE WHITE BLOOD CELLS

In animals below the amphioxus only white blood exists, and copper generally takes the place of iron in the circulating fluid. In the lowest vertebrates only traces of hemoglobin are to be

found. In the human fetus, at the earliest stage, only white blood exists. In the various types of leukemia there seems to be a pathologic reversion to the primitive condition.

Splenomyelogenous leukemia.—In splenomyelogenous leukemia there is an enormous increase of white blood cells, even to 500,000, or above, but these cells are without function, and have the malignant characteristics of large nuclei and enlarged nucleoli. The work of Wilson, MacCarty and Broders has shown that the large nucleus of the embryonic cell acts as the oxidizing agent, in obtaining nourishment for the rapidly dividing, as yet nonfunctioning cell, and that the large nucleolus establishes in the cell malignant characteristics.

In splenomyelogenous leukemia, the spleen, like all the lymphoid structures, is extremely susceptible to radium and x-ray, and this sensitivity renders these agents of first importance in palliation. There comes a time, however, when probably by reason of radiologic encapsulation of the spleen, they lose their effect. It has long been known that anything which will reduce the size of the spleen will reduce the percentage of the white blood cells, and that the red blood cells become greatly increased in number, with relief of the anemia. This fact has led us in forty-six cases to remove the spleen, which we found could be done quite readily after first reducing its size with x-ray and radium. Do not reduce below 30,000 for fear of toxic results.

These patients were all relieved temporarily, and a few are alive, although not cured, five, six, or more years after splenectomy.

In addition to these cases in which the disease was well marked, and there could be no doubt as to the diagnosis, the spleen has been removed in some atypical cases which, as cure resulted, have been classified in a subdivision of splenic anemia. In cases of younger persons, otherwise in good condition, and in the earlier stages of the disease, as well as in atypical cases, splenectomy may be considered in splenomyelogenous leukemia.

In the forty-six cases of splenomyelogenous leukemia in which splenectomy was performed, there were three deaths in the hospital.

FILTRATION OF INFECTIOUS AND TOXIC AGENTS

The strainer function of the spleen is well exemplified in the enlargements present in splenic anemia, tuberculosis, syphilis, typhoid fever and malaria.

Splenic anemia.—Splenic anemia is the most common type of splenomegaly in which splenectomy is performed. The spleen is large, the patient suffers from anemia, often intermittent, and when the disease is well developed, there often are hemorrhages from the stomach, pallor, weakness, great reduction of the hemoglobin and the red blood cells, and in the majority of cases a reduction of the white blood cells, often to 3500. Sometimes the white cells are increased rather than diminished, usually to not more than 10,000 or 12,000. In the late stages, described first by Banti in children, there may be cirrhosis of the liver, attended by ascites and other symptoms of hepatic insufficiency.

The cause of splenic anemia is not understood. The spleen shows an enormous amount of fibrosis, with atrophy of the pulp cells, and thrombophlebitis, perhaps the result of bacteria which have been strained out of the blood and destroyed, or toxic material which has failed to be detoxicated. The condition of the spleen resembles that to be found in certain chronic types of septic or syphilitic splenomegaly. Because the spleen in this condition usually is adherent and often extremely adherent, splenectomy may be difficult and attended with considerable risk. In the earlier cases with the patients in good condition, the risk is slight, but as patients even in the late stages, with cirrhosis of the liver, ascites, and marked hemorrhages, will often get well and remain well after the spleen is removed, the conscientious surgeon will remove the spleen in terminal conditions in which the risk is high.

It would appear that cirrhosis of the liver results from toxic material gathered in the spleen and sent to the liver, which the liver, failing to detoxicate, attempts to encapsulate diffusely, with the introduction of general fibrosis. The liver has the greatest power of regeneration of any organ in the human body. In the dog, by removing not more than a third of the liver at a time, the entire liver can be removed and will be replaced within the year.

In about 10 per cent of the cases in which recovery has taken place after splenectomy, the patients have died some time in the next ten years of hemorrhage from the stomach, probably from ruptured varices in the lower end of the esophagus. In our series of 148 cases, there were fourteen deaths following splenectomy.

Tuberculosis.—In nine cases of tuberculosis of the spleen the spleen was removed, with cure in five. One patient died from acute miliary tuberculosis, possibly due to rupture of tuberculous abscesses in the parenchyma, resulting in a vascular infection at the time of the operation. One could not be traced, and two patients have developed other manifestations of chronic tuberculosis.

Syphilis.—In ten cases of intractable syphilis with enlargement of the spleen, splenectomy was performed, with one death. In these cases the symptoms of chronic anemia were almost immediately relieved, and the Wassermann reaction on the blood became negative for the first time.

Typhoid fever has almost disappeared, and malaria is now under such good control by modern treatment as to give little occasion, in this country at least, for splenectomy for the relief of chronic splenomegalia of such origin.

SPLENIC NEOPLASMS

Benign tumors of the spleen are usually secondary in character, due to hemorrhage or injury. Benign lymphomas are also seen. In cases of this type splenectomy gives good results.

Primary malignant neoplasms are usually of the so-called lymphosarcoma type and vary greatly in malignancy, and not rarely may be

cured by splenectomy. In one case a very large lymphosarcoma of the spleen was removed. The patient, a young married woman, lived eight years and became the mother of three children. She died from metastasis.

In that curious disease described by Gaucher, in which the spleen is huge, with deposits of the specific round cells in the liver, the removal of the spleen early may result in remarkable palliation, lasting so many years as practically to amount to the cure of an otherwise intractable and ultimately fatal disease.

Secondary metastatic malignant tumors of the spleen are common and are not affected by radium and x-ray to a greater extent than malignant tumors elsewhere, because the cells are characteristic of the primary growth and not of the spleen.

In conclusion, a few words with regard to the splenectomy: Make an incision just to the left of the median line, or a transverse incision of adequate size. Carry out the two fundamental surgical requirements: See what you are doing and leave a dry field. As a last admonition, do not remove the spleen when the patient is on the down grade from the disease, but rather by means of transfusions and general preoperative care, start the patient on the up-grade before operating.

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ANOXEMIA*

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ON casting about for a subject it occurred to me that you would be interested in anoxemia—low oxygen and its effect on the flier.

During the last war, or rather during its later stages, combats at elevations of 18,000 and 20,000 feet were frequent. Since 1918 there have been great improvements in planes and engines. The supercharger in particular is coming into general use in military aviation, so that in future wars we may expect most of the aerial operations to be around the 25,000 and 30,000 foot levels. Anoxemia therefore is a subject of real practical significance to those of us now connected with the Air Corps and will be, no doubt, to many of you in event of another emergency. I am only going to touch upon the salient features and we will first review briefly the normal physiology of respiration and circulation.

The limits of established life on the earth today may be fixed at five miles above and one mile below sea level.

Life, whether in the sea, on land, or in the air, requires oxygen and nature has had to make the anatomical modifications necessary to obtain it in animals, birds, and fish.

In a wide sense respiration is the exchange of gases between a living substance and the medium in which it lives. In man this takes place in the blood through the lungs and depends upon the following physical factors:

1. Henry's law: The absorption of a gas by a liquid varies directly as the pressure.
2. The law of partial pressure: If a liquid be exposed to a mixture of gases it will absorb each gas in the proportions in which it exists in the mixture.

There are two other factors, namely: the temperature and the kind and quantity of salts in the liquid. These play but small part, so we will disregard them.

Man's respiratory system is adapted to the conditions obtaining at lea level, where the air contains about 21 per cent oxygen. In the depths of the lungs this percentage is reduced to about 15 per cent on account of dilution with residual air and water vapor. The partial pressure of the oxygen in the inspired air is reduced from 159 millimeters of mercury to 103 millimeters in the lung alveoli.

The reverse condition obtains as regards carbon dioxid: alveolar air containing about 4.5 per cent, and atmospheric air about .04 per cent; oxygen therefore diffuses inward and carbon dioxid outward.

There is a chemical ratio maintained at all times under normal conditions in the blood plasma between the carbonic acid and the sodium bicarbonates. The normal proportion is about three to sixty. If, for example, an individual exercises he produces more carbon dioxid, the carbonic acid is increased and the individual breathes more rapidly and deeply to wash out or eliminate the excess carbon dioxid and restore the normal equilibrium. The respiratory center in the brain stem which controls breathing is affected by a respiratory hormone, which is the H-ion concentration, and slight changes in this concentration cause stimulation or lack of stimulation, as the case may be.

This is a sketchy account of external respiration, but it suffices to make clear what is to follow.

ALTITUDE BLOOD CHEMICAL CHANGES*

Exposure to high altitude produces a deficient oxygenation of the blood (anoxemia) as follows:

As one ascends there is a gradual but constant lowering of pressure. At sea level, as we have seen, the oxygen pressure is about one-fifth of the atmospheric pressure (159 millimeters of mercury)—it is less in the lung alveoli; at 10,000 feet the oxygen pressure is reduced to 108 millimeters of mercury, and at 20,000 feet this pressure has been further reduced to only 74 millimeters. The diffusion of this gas is reduced directly as the pressure; consequently the blood's supply is insufficient and the condition of anoxemia exists. Concomitantly with the reduction of blood oxygen there is a decrease in the carbon dioxid. Oxygen want causes an increase in the rate and depth of respiration which washes the

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* Much of the material in the paragraphs on altitude blood changes and the body compensations has been taken from the published work of the Army School of Aviation Medicine and from Major L. H. Bauer's book "Aviation Medicine."